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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HIRIYANNA, KELAGINAMANE T

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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09/30/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No. 10/580,469	Applicant(s) KWON ET AL.	
	Examiner KELAGINAMANE T. HIRIYANNA	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7, 8 and 10-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7, 8 and 10-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/19/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response filed on 03/19/2009 in response to office action mailed on 11/19/2008 has been acknowledged.

Claims 7, 8 and 10-13 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

Withdrawn: Claims 7, 8 and 10-13 stand rejected under 102(a) as being anticipated by Ha et al., (2003, Calcified Tissue International, 72: 395) for the reasons of record as set forth in the office action mailed on 1/19/2008 is withdrawn in view of Applicants arguments in the response of 03/19/2009 and further in view of 35USC103 rejection promulgated below.

Withdrawn: Claims 7, 8 and 10-13 are rejected under 102(b) as being anticipated by Ha et al., (2002, Korean Patent Publication No: 1020020044745 A; published on 06/19/2002; art of record) for the reasons of record as set forth in the office action mailed on 11/19/2008 is withdrawn in view of Applicants arguments in the response of 03/19/2009 and further in view of 35USC103 rejection promulgated below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7, 8 and 10-13 are rejected under 35 USC 103 (a) as being unpatentable over Ha et al., (2002, Korean Patent Publication No: 1020020044745 A; published on 06/19/2002; art of record) in view of Spelsberg et al (1999, Mol. Endocrinol. 13:819-828; art of record) and Suh et al (2003, Phytochemistry 63:209-215; art of record).

The above claims are drawn to a method of preventing or treating metabolic bone disease comprising administering Sophorae fructus to a subject in need and in further

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limitation said disease is osteoporosis and treated by stimulating osteoblast proliferation, the secretion of growth factors and generation of nitric oxide in the osteoblast wherein the growth factor is IGF-1 or TGF-beta and further inhibiting secretion of cytokines such as IL-1 or IL-6 or osteoclast differentiation.

Regarding claims 7, 8, and 10 Ha teaches a method of preventing or treating bone loss and osteoporosis by orally administering herbal extract from Sophorae flos (Abstract). Ha teaches that the herbal extract contained ample quantities of phytoestrogen (genestein), consumption which has been shown prevent bone loss by stimulating osteoblastic bone formation and preventing osteoclastic bone resorption in the prior art. Sophorae fructus being a closely related to above species of Sophorae (both belong to leguminosae plant family), it is obvious that it too comprised the same bone therapeutic principles in its extract. Absent reason to believe otherwise the secretion of growth factors IGF-1 or TGF-beta involved in bone reformation and inhibition of bone resorptive cytokines occur and the disease is prevented or treated. Ha however, does not disclose the details of the molecular mechanisms behind phytoestrogen action in the abstract.

Spelsberg however, teaches regarding the limitations in claim 10-13 regarding the cellular mechanisms associated with estrogen mediated bone therapy (entire article, abstract; Fig.1; Fig.3; Table.1; p.626) wherein he teaches stimulating osteoblast proliferation, secretion of growth factors IGF-1 and TGF-beta1 and decrease of IL-1beta and IL-6 and inhibition of osteoclast differentiation (entire article, abstract; Fig.1; Fig.3; Table.1; p.626).

Suh et al teaches that the phytohormone genistein (present in Leguminosae plants such as Soybeans) treatment of osteoblast cells causes inhibition of their TNF induced apoptosis by decreasing IL-6 but did not decrease nitric oxide (NO) (abstract; Fig.4; p.213, col.1, paragraphs 3-4 bridging col.2).

Thus it would have been obvious for one of ordinary skill in the art to substitute in the Ha's method of treating osteoporosis with the phytoestrogens derived from Sophorae flos, the extracts of Sophorae fructus species and further include the steps of analyzing their effects on osteoblasts and osteoclasts for the increase or decrease of the marker factors including IGF-1, cytokines including IL-6 and NO production to quantitatively

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determine the bone growth as further taught by Suh and Spelsberg. One of ordinary skill in the art would have reasonable expectation of success making using extracts from plant species *Sophorae fructus* for treating osteoporosis in subjects in need and further quantitate its cellular effects in bone growth and resorption because art teaches that making and using of the extracts from closely related leguminous plants like *Sophorae flos* and soybean species for treating osteoporosis is routine. Thus, the claimed invention was *prima facie* obvious.

Claims 7, 8 and 10-13 are rejected under 35 USC 103 (a) as being unpatentable over Ha et al., (2003, *Calcified Tissue International*, 72: 395; art of record) in view of Spelsberg et al (1999, *Mol. Endocrinol.* 13:819-828; art of record)) and Suh et al (2003, *Phytochemistry* 63:209-215; art of record).

The above claims are drawn to a method of preventing or treating metabolic bone disease comprising administering *Sophorae fructus* to a subject in need and in further limitation said disease is osteoporosis and treated by stimulating osteoblast proliferation, the secretion of growth factors and generation of nitric oxide in the osteoblast wherein the growth factor is IGF-1 or TGF-beta and further inhibiting secretion of cytokines such as IL-1 or IL-6 or osteoclast differentiation.

Regarding above claims Ha teaches a method of preventing or treating bone loss and osteoporosis by orally administering herbal extracts from *Sophorae flavescentis* and *sophorae flos* (Abstract). Ha further teaches that *sophorae flos* belongs to plant family Leguminosae (Abstract) and thus is closely related to *Sophorae fructus* of the instant invention. Ha further teaches such administration induced proliferation of osteoblast like cell (Abstract). Ha teaches that the herbal extract contained ample quantities of phytoestrogen (genestein), consumption which has been shown prevent bone loss by stimulating osteoblastic bone formation and preventing osteoclastic bone resorption in the prior art. *Sophorae fructus* being a closely related to above species of *Sophorae flos*, it is expected that *Sophorae fructus* too comprises of same or similar bone therapeutic principles in its extract. Absent reason to believe otherwise the secretion of growth

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factors IGF-1 or TGF-beta involved in bone reformation and inhibition of bone resorptive cytokines occur and the disease is prevented or treated

Spelsberg however, teaches regarding the limitations in claim 10-13 regarding the cellular mechanisms associated with estrogen mediated bone therapy (entire article, abstract; Fig.1; Fig.3; Table.1; p.626) wherein he teaches stimulating osteoblast proliferation, secretion of growth factors IGF-1 and TGF-beta1 and decrease of IL-1beta and IL-6 and inhibition of osteoclast differentiation (entire article, abstract; Fig.1; Fig.3; Table.1; p.626).

Suh et al teaches that the phytohormone genistein (present in Leguminosae plants such as Soybeans) treatment of osteoblast cells causes inhibition of their TNF induced apoptosis by decreasing IL-6 but did not decrease nitric oxide (NO) (abstract; Fig.4; p.213, col.1, paragraphs 3-4 bridging col.2).

Thus it would have been obvious for one of ordinary skill in the art to substitute in the Ha's method of treating osteoporosis with the phytoestrogens derived from Sophorae flos, the extracts of Sophorae fructus species and further include the steps of analyzing their effects on osteoblasts and osteoclasts for the increase or decrease of the marker factors including IGF-1, cytokines including IL-6 and NO production to quantitatively determine the bone growth as further taught by Suh and Spelsberg. One of ordinary skill in the art would have reasonable expectation of success making using extracts from plant species Sophorae fructus for treating osteoporosis in subjects in need and further quantitate its cellular effects in bone growth and resorption because art teaches that making and using of the extracts from closely related leguminous plants like Sophorae flos and soybean species for treating osteoporosis is routine. Thus, the claimed invention was *prima facie* obvious.

Response to Applicants Arguments of 03/19/2009:

The Applicant argues that the source of the plant extracts taught in the cited prior art of Ha et al (2002, Korean patent publication) and Ha et al (2003, Calcified Tissue International, 72: 395; art of record) are not related to the plant Sophorae fructus of instant

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invention and submits non-scientific publications that discloses *Sophorae flaventis* belongs to a different family of plants,

The Applicants arguments are however found not persuasive because even excluding *Sophorae flaventis* from the equation, it is clear from the Has publication that *Sophorae flos* in fact belongs to leguminosae family of plants and hence is closely related species of *Sophorae fructus* of instant invention which has been disclosed as a leguminous plant. Further art provides ample evidence that other leguminous plants such as soybeans clearly comprise several phytoestrogen compounds which possess the effective properties of estrogen in treating osteoporosis and other related bone diseases. Hence an obviousness rejection is promulgated as above. The Applicant further should note that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992).

Conclusion:

No claim allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension

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fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanne Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/
Primary Examiner, Art Unit 1633